

PATENT
10/023,969
Docket 084/002

REMARKS

This paper is responsive to the Office Action dated July 15, 2003, which is the second action on the merits of the application. The action has been made final

Claims 1-25 are pending in the application; claims 1-4, 7, 9-11, and 16-17 are indicated as being under examination, with the others withdrawn from consideration. Please note that claims 20, 22, and 23 depend from claim 16 in the same manner as claims 7, 9, and 10 depend from claim 1. Accordingly, the claims under examination should include claims 1-4, 7, 9-11, 16-17, 20, and 22-23.

Several grounds of rejection have been withdrawn, and claims 4 and 17 are allowed, for which applicant is grateful.

Claim 3 is indicated as being rejected, but no reasons are given in the Office Action to substantiate the rejection. Applicant hereby requests confirmation that this claim is in condition for allowance. Claims 1, 2, 7, 9-11, and 16 stand variously rejected, and are discussed below.

Further consideration and allowance of the application is respectfully requested.

Request to remove finality of rejection

Applicant respectfully submits that the claims under examination (claims 1-4, 7, 9-11, 16-17, 20, and 22-23) are in condition for allowance.

However, in the event the Examiner determines there are additional matters to be addressed, applicant requests that the finality of the Office Action be withdrawn as premature, pursuant to MPEP § 706.07(d).

The Office Action rejects certain claims in the application under 35 USC § 102, § 103, and the doctrine of double patenting over a combination of an abstract by Pham et al. (General Meeting of the Amer. Soc. for Microbiology, 1999) with other references. These are all new rejections, since the Pham reference has not previously been cited. However, the Pham reference has been under consideration by the Office at least since the filing of the Information Disclosure Statement in this application on December 4, 2002, which was more than four months before the first Office Action on the merits of this application. These rejections could all have been made with respect to claims 7 and 9-11 in the first Office Action.

MPEP § 706.07(a) indicates that subsequent Office Actions should not be made final, where the examiner introduces a new ground of rejection not necessitated by applicant. Removal of finality is therefore requested.

PATENT
10/023,969
Docket 084/002

Rejections under 35 USC § 103 and Double Patenting:

Claims 1, 2, 7, 9-11 and 16 stand rejected under § 103 with respect to a combination of the Pham reference with a patent application by Schiff (US 2002/0128221 A1).

Claims 1, 2, 7, and 9-11 also stand rejected under the judicially created doctrine of obviousness-type double patenting, with respect to the Pham reference in combination with copending application USSN 09/994,427 (the Schiff application).

These are new rejections. The Office Action indicates that it would be obvious to use a tissue specific promoter as taught by Schiff with the cytopathic virus taught by Pham et al.

Applicant respectfully disagrees for two reasons.

First, there is no clear indication in the abstract that a cytopathic virus was constructed. This is a one-page abstract, which itself is inadequate to enable the skilled reader to perform the process¹. At the bottom of the abstract, there is an proposal for possible construction of human CMV construct containing IE1 or IE2 in the context of ecdysone inducible E1 and E3 deletions (whatever that is). It says that the Invitrogen system was used to insert HCMV IE2 into the vector "without inducing it", yielding viral constructs that "did not plaque". This experiment lacks a positive control showing the vector was actually constructed, by making plaques *in the presence of* the ecdysone hormone switch. Furthermore, the abstract earlier indicates that the AN cell line was E1 positive, *which should complement the E1a deficiency* in the virus, allowing it to plaque *whether or not* the HCMV genes were in the construct.

Thus, there is certainly no clear controlled experiment showing that Pham et al. successfully made any viral construct containing an HCMV gene, nor has the undersigned been able to find any evidence that this work has been published in a peer-reviewed journal. A prior art reference must be enabling for the invention it is cited against². This abstract is inadequate to enable even the experiment it purports to describe.

¹ A one-page promotional brochure boasting of the ability and the results of a process is insufficient as a matter of law to constitute an enabling disclosure of that process. *Reading & Bates Construction Co. v. Baker Energy Resources Corp.*, 223 USPQ 1168 (Fed. Cir. 1984).

² "[T]he prior art reference must be enabling, thus placing the allegedly disclosed matter in the possession of the public." *Akzo N.V. v. U.S. Int'l Trade Comm'n*, 1 USPQ2d 1241 (Fed. Cir. 1986), cert. denied, 482 U.S. 909 (1987). "[T]he reference must be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *In re Paulsen*, 31 USPQ2d 1671 (Fed. Cir. 1994).

PATENT
10/023,969
Docket 084/002

Second, the objective of the Pham abstract is *not* to make a cytopathic virus for treating cancer. Instead, it makes the point that adenovirus vectors designed to be replication incompetent for the purpose of gene therapy, may nevertheless be capable of replicating in the large proportion of the population that have a history of HCMV infection (Pham abstract, 2nd sentence). The obvious implication is that adenovirus vectors designed for gene therapy should be crippled further than just having an E1a deletion, so as to be replication incompetent (and therefore safe) for all potential recipients, regardless of their history with HCMV.

This contrasts with the objective of the invention claimed in the present patent application, which is to provide a virus that is replication competent in cancer cells. This also contrasts with the objective of the Schiff application, which is to provide a vector that causes expression of foreign antigen in cancer cells. In fact, the primary objective of the Schiff invention is not to kill cancer cells by viral replication, but by causing cancer cells to express an antigenic carbohydrate, which results in lysis of the cancer cell by naturally occurring antibody in the host. There would be no reason to put a tissue or tumor-specific transcriptional control element into the vectors of Pham alongside a heterologous gene that supports viral replication, since the entire purpose of Pham is to *eliminate* the potential for viral replication, and thereby allow the vector to be used safely in all cells in all patients.

There is no motivation to combine two references in support of a § 103 rejection when the substitution causes the product in the Pham reference to work against its intended purpose³.

Withdrawal of this rejection is respectfully requested.

Rejections under 35 USC § 102:

Claims 1, 2, 7, and 9-11 stand rejected under § 102(a) as being anticipated by a combination of the Pham reference and a patent application by Morin et al. (WO 00/46355). Claims 1, 2, 7, and 11 stand rejected under § 102(b) as being anticipated by a combination of the Pham reference and a patent by Henderson et al. (U.S. 5,871,726).

Applicant respectfully disagrees. None of these references by themselves teach a replication-conditional or replication competent adenovirus having both a tissue or tumor specific transcriptional control element, and a heterologous gene that replaces a function of an adenovirus E1a gene.

³ If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 123 USPQ 349 (CCPA 1959). If promised modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984).

PATENT
10/023,969
Docket 084/002

Since none of the claims are anticipated by any species in any one reference, the claims are patentable under 35 USC § 102. Furthermore, the Pham reference cannot justifiably be combined with Morin or Henderson, for the same reasons that it cannot be combined with the Schiff reference. Withdrawal of these rejections is respectfully requested.

Request for Rejoinder:

As explained above, the claims under examination should constitute claims 1-4, 7, 9-11, 16-17, 20, and 22-23.

Applicant hereby renews the request for rejoinder previously presented in the paper filed in this application on February 21, 2003.

Claim 1 is generic to all the species in groups A to E, and groups F to R. Accordingly, the non-elected species can be rejoined into the group under examination upon determination that claim 1 is patentable. This has the effect of rejoining claims 3, 5-11, and 18-23 into the application in their entirety.

Claims 12-15 are method claims that depend from and incorporate the limitations of product claims 1-11. Claims 24-25 are method claims that depend from and incorporate the limitations of product claims 16-23. Applicant hereby requests that these claims (and all other method claims depending from product claims in the elected group) be rejoined, upon determination that the product claims are patentable, in accordance with MPEP § 821.04.

Request for Interview

Applicant respectfully requests that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

In the event that the Examiner determines that there are other matters to be addressed, applicant hereby requests an interview by telephone.

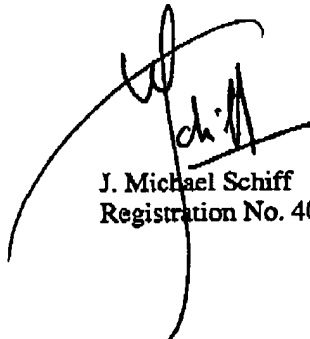
Fees Due

Enclosed with this Amendment is authorization to charge the Deposit Account for the amendment to claim 4, which increases the number of independent claims in this application.

PATENT
10/023,969
Docket 084/002

Should the Patent Office determine that a further extension of time or any other relief is required for further consideration of this application, applicant hereby petitions for such relief, and authorizes the Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



J. Michael Schiff
Registration No. 40,253

GERON CORPORATION
230 Constitution Drive
Menlo Park, CA 94025
Telephone: (650) 473-7715
Fax: (650) 473-8654

July 29, 2003